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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 05/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,996	ECKER ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,14,17 and 28-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10, 14, 17, 28-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

DETAILED ACTION

Status

Claims 1-10, 14, 17, 28-44 are pending.

Claims 1-10, 14, 17, 28-44 are rejected.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Priority

1. While this application claims priority to a variety of parent applications, claim 3 is not supported by the earliest parent applications, such as 09/798,007. Claim 3, drawn to air samples, appears to lack any support in 09/798,007.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1are rejected under 35 U.S.C. 102(b) as being anticipated by Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712).

Muddiman teaches a method of determining a genotype of a bioagent (see page 1546 and 1547, column 1, where a G to C change in the B. subtilis sequence was determined), comprising:

(a) selecting at least one pair of oligonucleotide primers, wherein one member of said pair of primers hybridizes to a first conserved region of nucleic acid encoding a ribosomal RNA and the other member of said pair of primer hybridizes toa second conserved region of nucleic acid encoding ribosomal RNA wherein said first and second conserved regions flank a variable nucleic acid region which varies among bioagents (see page 1544, where the PCR methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches selection of conserved primers at page 3708, column 1, paragraph 2 with a variable region between the conserved primers),

(b) amplifying nucleic acid from one or more bioagents with said pair of oligonucleotide primers to produce an amplification product (see page 1544, where the PCR methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches PCR amplification at page 3707, column 1, subheading "polymerase chain reaction"),

(c) determining the molecular mass of said amplification product by mass spectrometry (see page 1544, where the mass spectrometry methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches mass spectrometry at page 3707, column 2, subheading "Mass spectrometry"),

(d) calculating the base composition of said amplification product from said molecular mass (see table 1, where base composition was determined and see page 1547, column 1, where the first ranked mass was consistent with DNA sequencing results),

(e) comparing said base composition to calculated or measured base compositions of amplification products of known bioagents produced by using said pair of oligonucleotide primers, thereby identifying the unknonw bioagent at the species level (see table 1, where Muddiman shows the expected base composition and the calculated base composition for each of B. thuringiensis and B. subtilis, thereby determining the species of each amplification product)

With regard to claims 2, 7, Muddiman (Anal. Chem. (1996) 68:3705-3712) teaches the use of samples from nutrient broth (see page 3707, column 1).

With regard to claim 14, Muddiman teaches ESI-TOF mass spectrometry (see page 1543, column 2).

With regard to claim 17, Muddiman teaches detection of bacteria (see table 1).

With regard to claim 29, Muddiman shows the expected base composition and the calculated base composition for each of B. thuringiensis and B. subtilis, thereby determining the species of each amplification product (see table 1).

With regard to claim 30, Muddiman teaches identifying a sub-species characteristic of said bioagent, thereby determining the genotype of said bioagent (see page 1546, column 2 and page 1547, column 1, where a G to C change was detected in the B. subtilis sequence relative to the prior art sequence, demonstrating the presence of a specific B. subtilis genotype and consequently a specific sub species characteristic).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 2, 6-8, 14, 17 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Koster (WO 98/20166).

Muddiman teaches a method of claim 1 of identifying a bioagent in a sample (see abstract), comprising:

(a) selecting at least one pair of oligonucleotide primers, wherein one member of said pair of primers hybridizes to a first conserved region of nucleic acid encoding ribosomal RNA and the other member of said pair of primers hybridizes to a second

conserved region of nucleic acid encoding ribosomal RNA wherein said first and second regions flank a variable nucleic acid region that varies among bioagents (see page 3707, column 1, where the primers are drawn to the 16S and 23S rRNA sequences, which are conserved to permit amplification from two different species whcih have a variable length region in between the two primers and see page 3707, column 2),

(b) amplifying nucleic acid from said one or more bioagents with said pair of oligonucleotide primers to produce an amplification product (see page 3707, column 1, subheading “polymerase chain reaction”),

(c) determining the molecular mass of said amplification product by mass spectrometry (see page 3707, column 2 to page 3708, subheading “Mass spectrometry”)

With regard to claims 2, 6-8, Muddiman teaches samples in a container in a building which is a sample from an “environment” and which is a product (see page 3707, column 1).

With regard to claims 14, Muddiman uses FT-ICR mass spectrometry with ESI (see page 3707, column 2).

With regard to claim 17, Muddiman teaches that the bioagent is a Bacilli bacterium (see abstract).

With regard to claim 28, Muddiman teaches determinations at the Genus level between the Bacillus cereus group and the Bacillus subtilis group (see page 3707, column 1).

Muddiman teaches using FT-ICR-MS to analyze and compare the PCR products but does not teach base composition signatures.

Koster expressly teaches comparison of base compositions with both modified and unmodified products (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Koster in the analytical method of Muddiman since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line

26 to page 76, line 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Muddiman with the base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

6. Claims 1-2, 8-9, 14, 17 and 29, 31-32, 35-38, 41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al (U.S. Patent 6,001,564) in view of Koster (WO 98/20166).

Bergeron teaches a method of claim 1 of identifying a bioagent in a sample (see abstract), comprising:

(a) selecting at least one pair of oligonucleotide primers, wherein one member of said pair of primers hybridizes to a first conserved region of nucleic acid encoding ribosomal RNA and the other member of said pair of primers hybridizes to a second conserved region of nucleic acid encoding ribosomal RNA wherein said first and second regions flank a variable nucleic acid region that varies among bioagents (see column 9, lines 15-25 and see column 34, Annex IV),

(b) amplifying nucleic acid from said one or more bioagents with said pair of oligonucleotide primers to produce an amplification product (see column 7, lines 29-54),

(c) determining the molecular mass of said amplification (see column 7, lines 55-56)

With regard to claims 2, 8-9, 32, 37-38, Bergeron teaches the use of environmental samples including food samples (see claim 2)

With regard to claim 17, 41, Bergeron teaches that the bioagent is any of a variety of bacteria (see column 19, for example).

With regard to claim 29, 43, Bergeron teaches species specific amplification (see column 7, line 31 and column 14, example 12).

With regard to claim 31, Bergeron teaches amplification using primers drawn to a variety of proteins including replication (see column 9, lines 25-30, "Well-conserved bacterial genes other than ribosomal RNA genes could also be good candidates for universal bacterial detection directly from clinical specimens. Such genes may be associated with processes essential for bacterial survival (e.g. protein synthesis, DNA synthesis, cell division or DNA repair").

Bergeron does not teach mass spectroscopy for detection of the microorganisms.

In particular, Koster expressly teaches the use of MALDI-TOF for diagnosis of bacterial or viral infections (see pages 73-79). Koster exemplifies this analysis in Example 5.

Koster expressly teaches comparison of base compositions with both modified and unmodified products (see page 66, for example, as well as page 105, table II and pages 69-70). At page 105, table II, Koster provides the base composition of three different PCR products determined by MALDI-TOF. Further, Koster specifically discusses using base composition to analyze mutations as discussed on page 70, where Koster notes "MS can also be used to determined full or partial sequences of larger DNAs; this can be used to detect, locate, and identify new mutations in a given gene region."

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Koster in the analytical method of Bergeron since Koster states "In another embodiment, an accurate sequence determination of a relatively large target nucleic acid, can be obtained by generating specifically terminated fragments from the target nucleic acid, determining the mass of each fragment by mass spectrometry and ordering the fragments to determine the sequence of the larger target nucleic acid (see page 75, line 26 to page 76, line 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Bergeron with the base composition Mass spectrometric approach of Koster since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

7. Claims 1-2, 8-9, 14, 17 and 29, 31-32, 35-38, 41 and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Bergeron et al (U.S. Patent 6,001,564).

Muddiman teaches a method of determining a genotype of a bioagent (see page 1546 and 1547, column 1, where a G to C change in the B. subtilis sequence was determined), comprising:

(a) selecting at least one pair of oligonucleotide primers, wherein one member of said pair of primers hybridizes to a first conserved region of nucleic acid encoding a

ribosomal RNA and the other member of said pair of primer hybridizes toa second conserved region of nucleic acid encoding ribosomal RNA wherein said first and second conserved regions flank a variable nucleic acid region which varies among bioagents (see page 1544, where the PCR methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches selection of conserved primers at page 3708, column 1, paragraph 2 with a variable region between the conserved primers),

(b) amplifying nucleic acid from one or more bioagents with said pair of oligonucleotide primers to produce an amplification product (see page 1544, where the PCR methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches PCR amplification at page 3707, column 1, subheading "polymerase chain reaction"),

(c) determining the molecular mass of said amplification product by mass spectrometry (see page 1544, where the mass spectrometry methods are indicated as described in Muddiman et al (Anal. Chem. (1996) 68:3705-3712), which teaches mass spectrometry at page 3707, column 2, subheading "Mass spectrometry"),

(d) calculating the base composition of said amplification product from said molecular mass (see table 1, where base composition was determined and see page 1547, column 1, where the first ranked mass was consistent with DNA sequencing results),

(e) comparing said base composition to calculated or measured base compositions of amplification products of known bioagents produced by using said pair

of oligonucleotide primers, thereby identifying the unknonw bioagent at the species level (see table 1, where Muddiman shows the expected base composition and the calculated base composition for each of B. thuringiensis and B. subtilis, thereby determining the species of each amplification product)

With regard to claims 2, 7, Muddiman (Anal. Chem. (1996) 68:3705-3712) teaches the use of samples from nutrient broth (see page 3707, column 1).

With regard to claim 14, Muddiman teaches ESI-TOF mass spectrometry (see page 1543, column 2).

With regard to claim 17, Muddiman teaches detection of bacteria (see table 1).

With regard to claim 29, Muddiman shows the expected base composition and the calculated base composition for each of B. thuringiensis and B. subtilis, thereby determining the species of each amplification product (see table 1).

With regard to claim 30, Muddiman teaches identifying a sub-species characteristic of said bioagent, thereby determining the genotype of said bioagent (see page 1546, column 2 and page 1547, column 1, where a G to C change was detected in the B. subtilis sequence relative to the prior art sequence, demonstrating the presence of a specific B. subtilis genotype and consequently a specific sub species characteristic).

Muddiman does not teach all of the different sample sources or nucleic acid targets.

Bergeron teaches a method of claim 1 of identifying a bioagent in a sample (see abstract), comprising:

(a) selecting at least one pair of oligonucleotide primers, wherein one member of said pair of primers hybridizes to a first conserved region of nucleic acid encoding ribosomal RNA and the other member of said pair of primers hybridizes to a second conserved region of nucleic acid encoding ribosomal RNA wherein said first and second regions flank a variable nucleic acid region that varies among bioagents (see column 9, lines 15-25 and see column 34, Annex IV),

(b) amplifying nucleic acid from said one or more bioagents with said pair of oligonucleotide primers to produce an amplification product (see column 7, lines 29-54),

(c) determining the molecular mass of said amplification (see column 7, lines 55-56)

With regard to claims 2, 8-9, 32, 37-38, Bergeron teaches the use of environmental samples including food samples (see claim 2)

With regard to claim 17, 41, Bergeron teaches that the bioagent is any of a variety of bacteria (see column 19, for example).

With regard to claim 29, 43, Bergeron teaches species specific amplification (see column 7, line 31 and column 14, example 12).

With regard to claim 31, Bergeron teaches amplification using primers drawn to a variety of proteins including replication (see column 9, lines 25-30, "Well-conserved bacterial genes other than ribosomal RNA genes could also be good candidates for universal bacterial detection directly from clinical specimens. Such genes may be

associated with processes essential for bacterial survival (e.g. protein synthesis, DNA synthesis, cell division or DNA repair").

Bergeron does not teach mass spectroscopy for detection of the microorganisms.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to utilize the Mass spectrometry method of Muddiman in the analytical method of Bergeron since Muddiman notes "This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confiermation of the base composition of PCR products (see page 1549, column 2)." So an ordinary practitioner would have been motivated to detect the PCR products of Bergeron with the base composition Mass spectrometric approach of Muddiman since Muddiman teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis.

8. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al (U.S. Patent 6,001,564) in view of Koster (WO 98/20166) and further in view of Kohne et al (5,567,587).

Bergeron in view of Koster teach the limitations of claims 1 and 31 as discussed above.

Bergeron in view of Koster do not teach analysis of air samples.

Kohne teaches analysis of air sample for bacterial contamination (see column 40, lines 12-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect air samples as taught by Kohne for bacterial detection with the method of Bergeron in view of Koster since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and the legionella organism being detected by Kohne is an important environmental pathogen that is present in air or water. An ordinary practitioner would have been motivated to modify the method of Bergeron in view of Koster to analyze Legionella in air in order to determine whether this dangerous pathogen was present in a rapid and efficient way as Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

9. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Bergeron et al (U.S. Patent 6,001,564) and further in view of Kohne et al (5,567,587).

Muddiman in view of Bergeron teach the limitations of claims 1 and 31 as discussed above.

Muddiman in view of Bergeron do not teach analysis of air samples.

Kohne teaches analysis of air sample for bacterial contamination (see column 40, lines 12-17).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect air samples as taught by Kohne for bacterial detection with the method of Muddiman in view of Bergeron since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and the legionella organism being detected by Kohne is an important environmental pathogen that is present in air or water. An ordinary practitioner would have been motivated to modify the method of Muddiman in view of Bergeron to analyze Legionella in air in order to determine whether this dangerous pathogen was present in a rapid and efficient way as Muddiman notes "This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confiermation of the base composition of PCR products (see page 1549, column 2)."

10. Claims 4-7 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al (U.S. Patent 6,001,564) in view of Koster (WO 98/20166) and further in view of Hurst et al (Anal. Chem. (1998) 70:2693-2698).

Bergeron in view of Koster teach the limitations of claims 1 and 31 as discussed above.

Bergeron in view of Koster do not teach water or soil samples or swabs.

Hurst teaches a method of claims 1 and 20 of identifying a bioagent in sample (see page 2696, column 1), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 2695, table I, and page 2694, column 2, where primers were synthesized which amplified a conservative region of the pmoA gene from methanotrophs and see figures 2-4 where molecular mass is shown for bioagents)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figure 4 and page 2696, where the MALDI-TOF can distinguish different microorganisms amplified by the 56 base pair regions).

With regard to claims 2, 4, 5, Hurst teaches environmental samples including groundwater and soil samples (see page 2693, column 1).

With regard to claims 6, 7, Hurst teaches obtaining surface swab samples from a container in a building (see page 2694, column 2 "Chromosomal DNA was isolated from methanotrophic cultures grown on agarose plates.", where the plates are the container and are in a building.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect water and soil samples as taught by Hurst for bacterial detection with the method of Bergeron in view of Koster since both Hurst and Bergeron expressly teaches bacterial detection of organism that are present in

environmental samples and the methanotrophic being detected by Hurst play important roles in bioremediation. An ordinary practitioner would have been motivated by Hurst to detect these organisms in order to advance bioremediation.

Further, an ordinary practitioner would have been motivated by Bergeron to select primers from the rRNA genes in order to obtain a more universal primer which would permit simpler analysis of multiple organisms as discussed by Bergeron (see column 9, lines 1-33).

11. Claims 4-7 and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Bergeron et al (U.S. Patent 6,001,564) and further in view of Hurst et al (Anal. Chem. (1998) 70:2693-2698).

Muddiman in view of Bergeron teach the limitations of claims 1 and 31 as discussed above.

Muddiman in view of Bergeron do not teach water or soil samples or swabs.

Hurst teaches a method of claims 1 and 20 of identifying a bioagent in sample (see page 2696, column 1), comprising:

(a) determining a first molecular mass of a first amplification product of a first bioagent identifying amplicon from the sample (see page 2695, table I, and page 2694, column 2, where primers were synthesized which amplified a conservative region of the pmoA gene from methanotrophs and see figures 2-4 where molecular mass is shown for bioagents)

(b) comparing the first molecular mass to a second molecular mass of a second bioagent identifying amplicon (see page 2694, column 2, where identical primers were used to amplify multiple amplicons) wherein both first and second amplicons are correlative (see figure 4 and page 2696, where the MALDI-TOF can distinguish different microorganisms amplified by the 56 base pair regions).

With regard to claims 2, 4, 5, Hurst teaches environmental samples including groundwater and soil samples (see page 2693, column 1).

With regard to claims 6, 7, Hurst teaches obtaining surface swab samples from a container in a building (see page 2694, column 2 "Chromosomal DNA was isolated from methanotrophic cultures grown on agarose plates.", where the plates are the container and are in a building.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to detect water and soil samples as taught by Hurst for bacterial detection with the method of Muddiman in view of Bergeron since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and the methanotrophic being detected by Hurst play important roles in bioremediation. An ordinary practitioner would have been motivated to modify the method of Muddiman in view of Bergeron to analyze environmental samples in a rapid and efficient way as Muddiman notes "This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by

which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confiermation of the base composition of PCR products (see page 1549, column 2)."

12. Claims 10 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al (U.S. Patent 6,001,564) in view of Koster (WO 98/20166) and further in view of Romick et al (U.S. Patent 6,468,743).

Bergeron in view of Koster teach the limitations of claims 1 and 31 as discussed above.

Bergeron in view of Koster do not teach analysis of cosmetics.

Romick teaches analysis of cosmetic and food samples for bacterial contamination (see column 23, lines 51-65). Romick also teaches detection of molds (see column 7, line 40).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze cosmetics and food for bacterial or mold detection as taught by Romick with the method of Bergeron in view of Koster since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and the organisms being detected by Romick are important contaminants of food and cosmetics. An ordinary practitioner would have been motivated to modify the method of Bergeron in view of Koster to analyze bacteria or mold in food or cosmetics in order to determine whether dangerous pathogens are present in a rapid and efficient way as Koster teaches that Mass Spectrometry is

accurate and can improve the speed, mass accuracy and precision of the analysis (see abstract, for example).

13. Claims 10 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Bergeron et al (U.S. Patent 6,001,564) and and further in view of Romick et al (U.S. Patent 6,468,743).

Muddiman in view of Bergeron teach the limitations of claims 1 and 31 as discussed above.

Muddiman in view of Bergeron do not teach analysis of cosmetics.

Romick teaches analysis of cosmetic and food samples for bacterial contamination (see column 23, lines 51-65). Romick also teaches detection of molds (see column 7, line 40).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze cosmetics and food for bacterial or mold detection as taught by Romick with the method of Muddiman in view of Bergeron since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and the organisms being detected by Romick are important contaminants of food and cosmetics. An ordinary practitioner would have been motivated to modify the method of Muddiman in view of Bergeron to analyze bacteria or mold in food or cosmetics in order to determine whether dangerous pathogens are present in a rapid and efficient way as Muddiman notes "This approach uses accurate

mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confiermation of the base composition of PCR products (see page 1549, column 2)."

14. Claims 28-30 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bergeron et al (U.S. Patent 6,001,564) in view of Koster (WO 98/20166) and further in view of Vossen et al (International J. Food Microbiol. (1996) 33:35-49).

Bergeron in view of Koster teach the limitations of claims 1 and 31 as discussed above.

While Bergeron clearly teaches species level detection, Bergeron in view of Koster do not expressly teach detection of all levels of organisms including genus and subspecies or strain level.

Vossen teaches that PCR can be used to detect all levels "varying from genus to strain level depending on the systems used (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze food for bacterial spoilage as taught by Vossen with the method of Bergeron in view of Koster since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and since Vossen expressly indicates that "Discrimination between subspecies and strain level is

shown to be helpful for investigating routes and sources of contamination. Differentiatiation at the species level is demonstrated to be essential in order to design a highly specific detection system enabling to signalize a microorganism that belongs to a particular species (see abstract)." An ordinary practitioner would have been motivated to modify the method of Bergeron in view of Koster to analyze bacteria in food in order to determine which genus, species or subspecies is present in a rapid and efficient way since Vossen teaches PCR as the preferred analysis mode and since Koster teaches that Mass Spectrometry is accurate and can improve the speed, mass accuracy and precision of the PCR analysis (see abstract, for example).

15. Claims 28-30 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Muddiman et al (1997) 69:1543-1549) as evidenced by Muddiman et al (Anal. Chem. (1996) 68:3705-3712) in view of Bergeron et al (U.S. Patent 6,001,564) and further in view of Vossen et al (International J. Food Microbiol. (1996) 33:35-49).

Muddiman in view of Bergeron teach the limitations of claims 1 and 31 as discussed above.

Muddiman clearly teaches species level detection and suggests some subtype level detection. Bergeron clearly teaches species level detection. However, Muddiman in view of Bergeron do not expressly teach detection of all levels of organisms including genus and subspecies or strain level.

Vossen teaches that PCR can be used to detect all levels "varying from genus to strain level depending on the systems used (see abstract).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to analyze food for bacterial spoilage as taught by Vossen with the method of Muddiman in view of Bergeron since Bergeron expressly teaches bacterial detection of organism that are present in environmental samples and since Vossen expressly indicates that "Discrimination between subspecies and strain level is shown to be helpful for investigating routes and sources of contamination. Differentiatiation at the species level is demonstrated to be essential in order to design a highly specific detection system enabling to signalize a microorganism that belongs to a particular species (see abstract)." An ordinary practitioner would have been motivated to modify the method of Muddiman in view of Bergeron to analyze bacteria in food in order to determine which genus, species or subspecies is present in a rapid and efficient way since Vossen teaches PCR as the preferred analysis mode and since Muddiman notes "This approach uses accurate mass measurements and can be extended by the use of mass shifts induced by modified base PCR or postamplification modification, providing a rapid and accurate scheme by which to characterize PCR products of increasing size. This scheme should be particularly attractive for rapid confiermation of the base composition of PCR products (see page 1549, column 2)."

Double Patenting

16. Claims 1-10, 14, 17, 28-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/660,997 in view of Muddiman. Although the conflicting

claims are not identical, they are not patentably distinct from each other because the copending application claims represent a species of the current claims in which specific biowarfare organisms are selected. Muddiman teaches selection of Bacillus including bacillus anthracis. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the method of claims 1-28 of copending Application No. 10/660,997 with Muddiman in order to detect organisms of interest such as Anthrax.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Response to Arguments

18. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

The only rejection remaining from the previous action is the double patenting rejection over 10/660,997. This rejection is maintained since the claims remain obvious over each other. Applicant indicated that a terminal disclaimer had been filed but no terminal disclaimer is found in the application.

Conclusion

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637
5/11/06